AMENDMENTS TO THE DRAWINGS

The attached sheet of drawings includes changes to FIG. 18. This sheet, which includes FIG. 18, replaces the original sheet including FIG. 18.

Attachment: Replacement Sheet

REMARKS

Claims 1 – 55 are currently pending and under examination. By this amendment, claims 6, 7, 10 – 12, 16, 17, 20 – 22, 26, 27, 30 –32, 36, 37, 40 – 42 and 46-55 have been withdrawn from consideration. Claims 1, 13, 23, 33 and 43 have been amended. Claims 1, 13, 23, 33 and 43 are independent. Accordingly, by this amendment claims 1 – 5, 8, 9, 13 – 15, 18, 19, 23 – 25, 28, 29, 33 – 35, 38, 39 and 43 – 45 are currently pending and under examination.

Applicants have amended claim 33 by switching steps (b) and (c) to maintain consistency through the claims with regard to the addition of the "forward" primers and then the addition of the "reverse" primers. As such no new matter has been added. Applicants note that subsequent references to claims 33(b) or (c) are directed to the "switched" version as indicated in the amended claims

Applicants have amended claims 1(b), 13(b), 23(b), 33(b) and 43(a) to clarify that the primer is being added "under conditions where" the primer is "extended around the circle for multiple revolutions to form a single-stranded DNA molecule of repeating units complementary to the sequence of the circular probe." Support for these amendments can be found *inter alia* at paragraphs [00171] and [00173] and FIGS. 16 and 32 in the application as originally filed.

Applicants have amended claims 1(c) and 43(b) to clarify that "at least one" oligonucleotide primer pair is added. Support for these amendments can be found *inter alia* at paragraph [00189] and FIG. 32 in the application as originally filed.

Applicants have amended claims 1(c)(i), 13(b)(i), 13(c)(i), 23(b)(i), 33(c)(i) and 43(b)(i) to clarify that the first primer comprises a first sequence "on its 3' end." Support for these amendments can be found *inter alia* at FIGS. 20A and 33A in the application as originally filed.

Applicants have amended claims 1(f), 13(e), 23(e), 33(e) and 43(e) to clarify that the amplification products comprise "a sequence that is substantially identical to a sequence in the circular" probe or nucleic acid sequence. Support for these amendments can be found *inter alia* at paragraphs [00171], [00173] and [00174] and FIG. 32 in the application as originally filed.

Applicants have amended claims 13(d), 23(d) and 33(d) to clarify that the DNA polymerase lacks "3' to 5' exonuclease activity." Support for these amendments can be found *inter alia* at paragraphs [00172] and [00346] in the application as originally filed.

Applicants have amended claims 23(b) and 33(c) to clarify that the multiple oligonucleotide primer is a "complex." Support for these amendments can be found *inter alia* at paragraphs [00187] and [00188] in the application as originally filed.

Applicants have amended claim 43(c) to substitute "probe" for "nucleic acid sequence" to maintain proper antecedent basis. Accordingly, no new matter has been added.

Objection to the Drawings

Applicants are required pursuant to 37 CFR 1.85(a) to submit the drawings corrections within the time period set forth in the Office Action. Accordingly, Applicants submit herewith new Figure 18. New Figure 18 has been revised to overcome the objections set forth in the January 5, 2007 Office Action.

Applicants respectfully request that new Figure 18 be entered and that this objection be withdrawn.

Rejections under § 112, First Paragraph

As an initial matter the invention generally relates to RAM amplification of a circular oligonucleotide whereby a forward primer hybridizes to the circular oligonucleotide. It is understood that the forward primer may be a primer pair or a multiple oligonucleotide primer complex. Via primer extension and the use of an appropriate DNA polymerase, the forward primer extends around the circular oligonucleotide and produces a long single stranded DNA of repeating units having a sequence complementary to the sequence of the circular oligonucleotide. Reverse primers, which are substantially identical to a portion of the circular oligonucleotide (and thus complementary to the long single stranded DNA), hybridize to the long single stranded DNA and via primer extension produce DNA molecules that are substantially identical to a sequence in the circular oligonucleotide. It is understood that the reverse primer may be a primer pair or a multiple oligonucleotide primer complex.

Page 2 of the January 5, 2007 Office Action states that claims 1 – 5, 8, 9, 13 – 15, 18, 19, 23 – 25, 28, 29, 33 – 35, 38, 39 and 43 – 45 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for amplifying a circular oligonucleotide using the method recited in claims 1 – 5, 8, 9, 13 – 15, 18, 19, 23 – 25, 28, 29, 33 – 35, 38, 39 and 43 – 45, does not reasonably provide enablement for detecting a target nucleic acid in a sample using the methods recited in claims 1 – 5, 8, 9, 13 – 15, 18, 19, 23 – 25, 28, 29, 33 – 35, 38, 39 and 43 – 45.

Specifically, the Office Action states on page 3 that although steps (b) and (c) of claim 1 require that at least one forward primer comprises a sequence complementary to a portion of the circular oligonucleotide probe and an oligonucleotide primer pair comprises a first primer comprising a first sequence that is substantially identical to a portion of the circular oligonucleotide probe, since claim 1 does not indicate that the at least one forward primer

comprising a sequence is complementary to which portion of the circular probe and the first primer of the primer pair comprising a first sequence is substantially identical to which portion of the circular probe and does not require that the second primer be complementary to the circular probe, it is unclear whether the product amplified from the circular probe contains a nucleotide sequence that is complementary to the first or second primer.

In order to expedite the prosecution of the subject application, and without conceding either the correctness of the Office Action's position or the need for amendment for patentability reasons, Applicants have amended claim 1(b) to clarify that the primer is being added "under conditions where" the primer is "extended around the circle for multiple revolutions to form a single-stranded DNA molecule of repeating units complementary to the sequence of the circular probe."

Applicants note that the second primer of the oligonucleotide primer pair binds only to the first primer of the oligonucleotide primer pair; it does not bind to the circular probe or the single-stranded DNA molecule produced from the primer extension of the forward primer. The first primer of the oligonucleotide primer pair acts as a "reverse primer" and binds to the single-stranded DNA molecule and via primer extension produces an amplification product that is substantially identical to the circular probe. Applicants have also amended claim 1(f) to clarify that the amplification products comprise "a sequence that is substantially identical to a sequence in the circular probe." Applicants respectfully request that this rejection be withdrawn.

Page 4 of the Office Action states that although step (a) of claims 13 or 23 requires contacting the target nucleic acid with a circular probe under conditions that allow hybrization between complementary sequences in the target nucleic acid and the circular probe and the

claims do not require that the polymerase lacks 3' to 5' exonuclease activity, it is possible that the target nucleic acid is cleaved due to 3' to 5' exonuclease activity.

In order to expedite the prosecution of the subject application, and without conceding either the correctness of the Office Action's position or the need for amendment for patentability reasons, Applicants have amended claims 13(d) and 23(d) to clarify that the DNA polymerase lacks "3' to 5' exonuclease activity." Accordingly, Applicants respectfully request that these rejections be withdrawn.

The Office Action states on page 5 that although steps (b) and (c) of claim 33 require that at least one forward primer comprises a sequence complementary to a portion of the circular oligonucleotide probe and a multiple oligonucleotide primers comprises a first primer comprising a first sequence that is substantially identical to a portion of the circular oligonucleotide probe, since claim 33 does not indicate that the at least one forward primer comprising a sequence is complementary to which portion of the circular probe and the first primer comprising a first sequence is substantially identical to which portion of the circular probe and does not require that the second primer or third primer of the multiple oligonucleotide primer be complementary to the circular probe, it is unclear whether the product amplified from the circular probe contains a nucleotide sequence that is complementary to the first or second or third primer of the multiple oligonucleotide primer.

In order to expedite the prosecution of the subject application, and without conceding either the correctness of the Office Action's position or the need for amendment for patentability reasons, Applicants have amended claim 33(b) to clarify that the primer is being added "under conditions where" the primer is "extended around the circle for multiple revolutions to form a

single-stranded DNA molecule of repeating units complementary to the sequence of the circular probe." Applicants have also amended claim 33(c) to clarify that the multiple oligonucleotide primer is a "complex."

Applicants note that the second and third primers of the multiple oligonucleotide primer binds only to the first primer of the multiple oligonucleotide primer; they do not bind to the circular probe or the single-stranded DNA molecule produced from the primer extension of the forward primer. The first primer of the multiple oligonucleotide primer acts as a "reverse primer" and binds to the single-stranded DNA molecule and via primer extension produces an amplification product that is substantially identical to a sequence in the circular probe. Applicants have also amended claim 33(e) to clarify that the amplification products comprise "a sequence that is substantially identical to a sequence in the circular probe." Applicants respectfully request that this rejection be withdrawn.

Page 5 of the Office Action states that although steps (a) to (c) of claim 43 indicate that at least one forward primer comprises a sequence complementary to a portion of the circular oligonucleotide probe, an oligonucleotide primer pair comprises a first primer comprising a first sequence that is substantially identical to a portion of the circular oligonucleotide probe and at least one reverse primer comprising a sequence is substantially identical to a portion of the circular probe, since claim 43 does not require that the at least one forward primer comprising a sequence is complementary to which portion of the circular probe, the first primer of the primer pair comprising a first sequence is substantially identical to which portion of the circular probe, the at least one reverse primer comprising a sequence is substantially identical to which portion of the circular probe, and does not require that the second primer of the oligonucleotide primer pair or the at least one reverse primer is complementary to the circular probe, it is unclear

whether the product amplified from the circular probe contains a nucleotide sequence that is complementary to the first or second primer of the oligonucleotide primer pair or the at least one reverse primer.

In order to expedite the prosecution of the subject application, and without conceding either the correctness of the Office Action's position or the need for amendment for patentability reasons, Applicants have amended claim 43(b) to clarify that the primer is being added "under conditions where" the primer is "extended around the circle for multiple revolutions to form a single-stranded DNA molecule of repeating units complementary to the sequence of the circular probe."

Applicants note that the second primer of the oligonucleotide primer pair binds only to the first primer of the oligonucleotide primer pair; it does not bind to the circular probe or the single-stranded DNA molecule produced from the primer extension of the forward primer. The first primer of the oligonucleotide primer pair acts as a "reverse primer" and binds to the single-stranded DNA molecule and via primer extension produces an amplification product that is substantially identical to the circular probe. Applicants have also amended claim 43(e) to clarify that the amplification products comprise "a sequence that is substantially identical to a sequence in the circular nucleic acid sequence." Applicants respectfully request that this rejection be withdrawn.

Rejections under § 112, Second Paragraph

Page 7 of the January 5, 2007 Office Action states that claims 1 – 5, 8, 9, 13 – 15, 18, 19, 23 – 25, 28, 29, 33 – 35, 38, 39 and 43 – 45 are rejected under 35 U.S.C. § 112, second

paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants maintain that the amendments discussed herein address these rejections and respectfully request that these rejections be withdrawn.

CONCLUSION

Applicants respectfully submit that this application is in condition for allowance. Early and favorable action is earnestly solicited. No fee, other than the $225.00 fee for a two-month extension of time, is deemed necessary in connection with the filing of this Response. However, if any additional fee is due the amount of such fee may be charged to Deposit Account No. 19-4709. In the event that there are any questions, or should additional information be required, please contact Applicants' attorney at the number listed below.

Respectfully submitted,

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